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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,022	06/18/2007	Ching-Shih Chen	22727/04418	4927

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EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
09/24/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocket@calfee.com
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Office Action Summary	Application No.	Applicant(s)	
	10/597,022	CHEN ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/08 &1/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Status of Claims:

Claims 1-25 are pending.

Claims 1-25 are rejected.

DETAILED ACTION

1. Claims 1-25 are under consideration in this Office Action.

Priority

2. It is noted that this application is a 371 of PCT/US04/40211(12/01/04), which claims benefit of 601/526,348(12/02/03) .

Drawings

3. The drawings filed on 7/6/06 are accepted by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the phrase " Z is chosen from $\underline{(CH_2)_m}$ wherein m is 0-3 and $\underline{(CH)_2}$ "is is recited. This expression is vague and indefinite because the claim defines it first with the specific range of $(CH_2)_m$ and then, defines again with $\underline{(CH)_2}$. Appropriate correction is required.

In claim 1, the term " A is hydrocarbyl group " is recited. This expression is vague and indefinite because the claim does not elaborate what is meant by the term " hydrocarbyl group " , which may indicate any compounds having any range of the number of carbon and hydrogen in the compounds. Appropriate correction is required.

In claims 2, 4-5, 8 and 25 , the phrases "A comprises " and " R comprises" are recited. These expressions are vague and indefinite because the term" comprises" would mean that there would be additional components besides the description of the "A" or "R"; the skilled artisan in the art is unable to figure out what else is present in the description of the "A" or "R".

Appropriate correction is required.

In claims 2-5, 8 and 25 , the phrases "an aliphatic group " and " an aromatic group" are recited. These expressions are vague and indefinite because they do not have any range of the carbon atoms. Appropriate correction is required.

In claims 5 and 25, the phrase "substituted " is recited. This expression is vague and indefinite because in the absence of the specific moieties intended to effectuate modification by the "substitution" or attachment to the chemical core claimed, the term

"substituted" renders the claims in which it appears indefinite in all occurrences wherein applicants fails to articulate by chemical name, structural formula or sufficiently distinct functional language, the particular moieties applicants regards as those which will facilitate substitution, requisite to identifying the composition of matter claimed. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claim 18, the phrases " a method of inhibiting neoplastic cell proliferation in an animal " are recited. The specification falls short because data essential for treating all kinds of cancers is not described in the specification. Moreover, the claims set forth the treatment of cancer generally. However, there are more than 3000 cancers. Applicants

have not identified a specific compound capable of treating "cancers" broadly. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective anti-tumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task. See also, In re Joller, 206 USPQ 885(CCPA 1980). Therefore, the specification has failed to support enablement for the method for inhibiting neoplastic cell proliferation in an animal. Therefore, an appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of prostate , breast, lung, thyroid cancer, lymphocytic leukemia, does not reasonably provide enablement for all kinds of conditions susceptible to treatment such as any types of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to include any conditions susceptible to treatment negatively or positively ,any types of cancers, which are not represented in the invention commensurate in scope with these claims.

Although the claims are directed to the treatment of an animal subject to combat conditions susceptible to treatment negatively or positively, the specification falls short because data essential for treating the animal subject to combat all kinds of cancer conditions susceptible to treatment negatively or positively by means of administering the claimed compounds is not described in the specification.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claims 18-19 is described in the following:

18. A method of inhibiting neoplastic cell proliferation in an animal comprising administering a therapeutically effective amount of at least one inhibitor according to claim 1.

19. The method according to claim 18, wherein the animal is a human.

The State of the Prior Art

The state of the prior art is as followed:

Nakajima *et al.*, "FR901228, a potent antitumor antibiotic, is a novel histone deacetylase inhibitor." Exp Cell Res 241: 126-133 (1998)), and the depsipeptide FR901228 (Nakajima *et al.*, Exp Cell Res 241: 126-133 (1998)). Among these agents, short-chain fatty acids are the least potent inhibitors with IC_{50} in the mM range, as compared to that of μM or even nM for other types of HDAC inhibitors. Although the use of short-chain fatty acids in cancer treatment has been reported, their therapeutic efficacy has been limited by the low anti-proliferative activity, rapid metabolism, and non-specific mode of action.

There is no conclusive disclosure in the prior art that the histone deacetylase inhibitor having the formula disclosed in claim 1 has been approved for treating all kinds of cancerous conditions.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the application of the histone deacetylase inhibitor having the

formula disclosed in claim 1 would result in regulating gene transcription through the modulation of nucleosomal packaging of DNA in gene expression only; this kind of treatment can not translated to the possible treatment of any types of cancers.

Hence, in the absence of a showing of correlation between all kinds of cancerous conditions as capable of treatment by the histone deacetylase inhibitor having the formula disclosed in claim 1, one of skill in the art is unable to fully predict possible results from the administration of the claimed histone deacetylase inhibitor having the formula due to the unpredictability of the role of the histone deacetylase inhibitor conclusively useful in treating all kinds of cancerous conditions.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the histone deacetylase inhibitor having the formula disclosed in claim 1 can treat any disorder, such as a terminal cancer. However, the specification is silent and fails to provide guidance as to whether any cancer requires the presence of the histone deacetylase inhibitor having the formula for treatment, i.e. the specification fails to provide a

correlation between those abnormalities and the histone deacetylase inhibitor having the formula that would lead to the direction and guidance for those diseases.

The presence or absence of working examples

There is one compound 42 used for testing prostate , breast, lung, thyroid cancer, and lymphocytic leukemia in the examples (see pages 46-48) . Furthermore, there are no other examples for other kinds of cancerous conditions negatively or positively as well as their corresponding pharmacological data. Also, the specification fails to provide enough working examples as to how all kinds of cancerous conditions can be treated negatively or positively by the application of claimed histone deacetylase inhibitor having the formula, i.e. again, there is no correlation between the application of the of the histone deacetylase inhibitor having the formula and claimed all kinds of cancerous conditions.

The breadth of the claims

The breadth of the claims is that all histone deacetylase inhibitor having the formula can treat all kinds of cancerous conditions without sufficient evidence to prove the applicability of each of those of the histone deacetylase inhibitors having the formula negatively or positively.

The quantity of experimentation needed

The quantity of experimentation needed is large. One of skill in the art would need to determine which one of those claimed histone deacetylase inhibitors having the formula would be effective for treating all kinds of cancerous conditions in the

clinical settings and also would furthermore then have to determine whether the claimed compound would provide the treatment for all kinds cancerous conditions.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine whether or not all the claimed histone deacetylase inhibitors having the formula exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the all the claimed histone deacetylase inhibitor having the formula for the treatment of all kinds of cancerous. As a result, necessitating one of skill to perform an exhaustive search for which diseases can be treated by the claimed histone deacetylase inhibitor having the formula in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to

engage in undue experimentation to test which cancers can be treated by the compound encompassed in the instant claims, with no assurance of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 36-45 of copending Application No. 12/361,626. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the genus and species relationship.

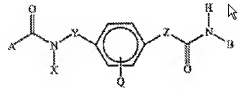
In the instant invention of claims 18-19, the followings are described :

18. A method of inhibiting neoplastic cell proliferation in an animal comprising administering a therapeutically effective amount of at least one inhibitor according to claim 1.

19. The method according to claim 18, wherein the animal is a human.

Whereas in the claims 26, 36,46,56 of the co-pending application, the followings are described:

Claim 36 (New): A method of inhibiting cancerous cell proliferation in an animal comprising: administering a therapeutically effective amount of a compound having the formula:



wherein:

X is chosen from H and CH_3;

Y is $(CH_2)n$ wherein n is 0-2;

Z is chosen from $(CH_2)_m$ wherein m is 0-3 and $(CH)_2$;

A is a hydrocarbyl group;

B is o-aminophenyl or hydroxyl group; and

Q is a halogen, hydrogen, or methyl, and

wherein the cancerous cell is selected from a group consisting of prostate cancer, lung cancer, acute leukemia, multiple myeloma, bladder carcinoma, renal carcinoma, breast carcinoma, colorectal carcinoma, neuroblastoma, and melanoma.

However, the instant invention differs from the co-pending application in that the neoplastic cell proliferation is unspecified .

Even so, the specification does disclose a generic teaching of cancer as well as many types of the cancers (see paragraph # 0144); furthermore, they are in a relationship between the genus and species regarding the types of the cancers although the rest of the claims are almost same with those of the copending application. In addition, the phrase "a method of inhibiting neoplastic cell proliferation in an animal" in the instant claim is analogous to the phrase "a method of inhibiting cancerous cell proliferation in an animal". Therefore, it would have been obvious to be motivated to modify the claimed invention of the co-pending application in order to broaden the generic treatment of the cancers since they have shared the common utility of the same compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

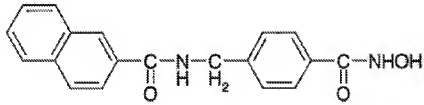
> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-5, 7-8, 16-20 are rejected under 35 U.S.C. 102(a) as being anticipated clearly by Sato (WO 03/070691).

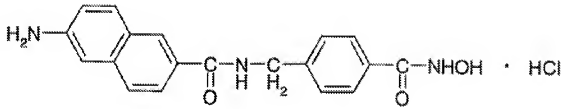
Sato discloses the followings(see abstract):

(57) Abstract: It is intended to provide a novel N-hydroxycarboxamide derivative which is excellent in physical properties such as stability and dissolution properties and a potent histone deacetylase (HDAC) inhibitory activity. It is found out that a novel N-hydroxycarboxamide derivative, which is obtained by using tranexamic acid as a lead compound, and its salt have a potent HDAC inhibitory activity. This N-hydroxycarboxamide derivative is useful in treating, relieving and preventing diseases concerning cell proliferation. In particular, it is expected that this derivative is highly efficacious as an anticancer agent or a carcinostatic agent. Moreover, it is expected that the above N-hydroxycarboxamide derivative is efficacious as an immunosuppressant or a gene therapy potentiator and usable in treating, relieving and preventing neurodegenerative diseases.

Also, the N-hydroxycarboxamide derivatives are described in the followings:



(see page 54) ,



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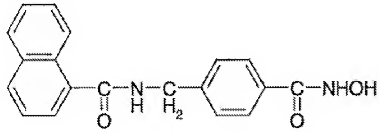
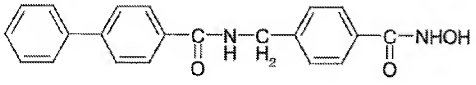
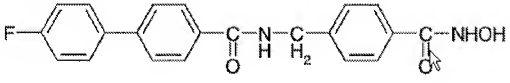
(see page 56)



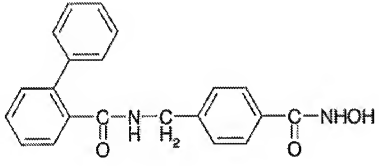
(see page 60),



(see page 63),



(see page 66),



(see page 70).

They are identical with the claims.

Claims 1-2, 7, and 16-17.,20 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by Bertolini et al (US 6,034,096).

Bertolini et al disclose the following compound(see col. 4, lines 24-26):

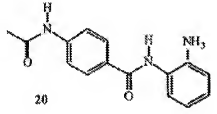
EXAMPLE 1

4-(5-Phenylpentanamido)benzohydroxamic acid

This is identical with the claims.

Claims 1-2 , 6, and 16-20 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by Manfred Jung (Current Medicinal Chemistry 2001, 8,1505-1511).

Manfred Jung discloses that the acetyldinaline as shown as # 20 is in clinical trials for the treatment of cancer(see page 1509):



20

This is identical with the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taylor Victor Oh/
Primary Examiner, Art Unit 1625
9/16/09